

```
chain nodes :
7 8 9 10 11 12 20 21
ring nodes :
1 2 3 4 5 6 13 14 15 16 17 18
chain bonds :
4-9 5-8 6-7 7-21 10-11 10-20
                               11-12
                                      11-13 20-21
ring bonds :
1-2 1-5 2-3 3-4
                 4-5
                      4-6 5-6
                               13-14
                                      13-18
                                            14-15
                                                  15-16 16-17
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 4-6 5-6 6-7 7-21 10-11 10-20
                                                      11-12 20-21
exact bonds :
4-9 · 5-8 11-13
normalized bonds :
13-14 13-18 14-15 15-16 16-17
                               17-18
```

STN Structure Search (Registry (Caplus)

10/552,456

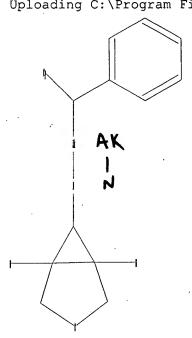
06/18/2007

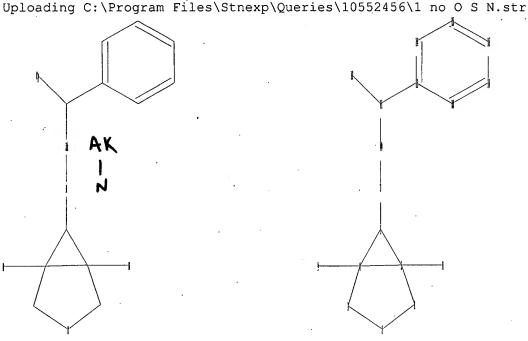
G1:0,S,N

Match level : 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 20:CLASS Generic attributes : 12: Saturation : Unsaturated

L1STRUCTURE UPLOADED

=>





chain nodes : 7 8 9 10 11 12 ring nodes : 1 2 3 4 5 6 13 14 15 16 17 18 chain bonds : 4-9 5-8 6-7 7-10 10-11 11-12 11-13 ring bonds : 1-2 1-5 2-3 3-4 4-5 4-6 5-6 13-14 13-18 14-15 15-16 16-17 17-18 exact/norm bonds : 1-2 1-5 2-3 3-4 4-5 4-6 5-6 6-7 7-10 10-11 11-12 exact bonds : 4-9 5-8 11-13 normalized bonds : 13-14 13-18 14-15 15-16 16-17 17-18

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom Generic attributes :

12:

Saturation

: Unsaturated

STRUCTURE UPLOADED L2

=> d 11

L1 HAS NO ANSWERS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT * Structure attributes must be viewed using STN Express query preparation.

=> s 11 SAMPLE SEARCH INITIATED 21:38:35 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 1447 TO ITE 1447 TO ITERATE

100.0% PROCESSED ✔ 1447 ITERATIONS SEARCH TIME: 00.00.01

1 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

COMPLETE BATCH

PROJECTED ITERATIONS: 26658 TO 31222

PROJECTED ANSWERS:

1 TO

80

L3 1 SEA SSS SAM L1

=> d scan

```
=> s 11 full
FULL SEARCH INITIATED 21:39:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED 27616 TO ITERATE
100.0% PROCESSED V 27616 ITERATIONS
                                                                        9 ANSWERS
SEARCH TIME: 00.00.01
            9 SEA SSS FUL L1
L4
=> d his
     (FILE 'HOME' ENTERED AT 21:37:38 ON 17 JUN 2007)
     FILE 'REGISTRY' ENTERED AT 21:37:56 ON 17 JUN 2007
                 STRUCTURE UPLOADED
L2
                 STRUCTURE UPLOADED
L3
               1 S L1
L4
               9 S L1 FULL
=> s 12
SAMPLE SEARCH INITIATED 21:39:16 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED 3002 TO ITERATE
 66.6% PROCESSED
                     2000 ITERATIONS
                                                                        2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                          BATCH **COMPLETE**
                             56754 TO 63326
PROJECTED ITERATIONS:
                                   2 TO
PROJECTED ANSWERS:
                                             163
```

2 SEA SSS SAM L2

L5

=> d scan

```
=> s 12 full

FULL SEARCH INITIATED 21:39:35 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED 58234 TO ITERATE

100.0% PROCESSED 58234 ITERATIONS

SEARCH TIME: 00.00.01

L6 35 SEA SSS FUL L2

=> d his

(FILE 'HOME' ENTERED AT 21:37:38 ON 17 JUN 2007)
```

35 ANSWERS

```
FILE 'REGISTRY' ENTERED AT 21:37:56 ON 17 JUN 2007
STRUCTURE UPLOADED
```

L1 STRUCTURE UPLOADED
L2 STRUCTURE UPLOADED
L3 1 S L1
L4 9 S L1 FULL
L5 2 S L2
L6 35 S L2 FULL

=> fil caplus **V** COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 344.65 344.86

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 21:39:48 ON 17 JUN 2007 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 17 Jun 2007 VOL 146 ISS 26 FILE LAST UPDATED: 15 Jun 2007 (20070615/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s 14 or 16 3 L4 8 L6 L7 8 L4 OR L6

=> d ibib abs hitstr 1-8

L7 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN
ACCESSION NUMBER: 2006:1226133 CAPLUS
DOCUMENT NUMBER: 145:505473
TITLE: Preparation of hydroxamic acids as histone

deacetylase

inhibitors for use against proliferative diseases

including cancers

Moffat, David Festus Charles; Patel, Sanjay Ratilal;
Mazzei, Francesca Ann; Belfield, Andrew James; Van

INVENTOR (S):

Meurs, Sandra Chroma Therapeutics Ltd, UK PCT Int. Appl., 120pp. CODEN: PIXXD2 PATENT ASSIGNEE(S):

DOCUMENT TYPE:

English FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PAT	ENT	NO.			KIN	D	DATE			APPL	I CAT	ION	NO.		D.	ATE	
						-									-		
WO 2006123121					A1 20061123			1	WO 2	006~	20060515						
	W:	AE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	ΈΥ,	BZ,	CA,	CH,
_																	
													,		,		
	RW:	AT.	BE.	BG.	CH.	CY.	CZ.	DE.	DK.	EE.	ES.	FI.	FR.	GB.	GR.	HU.	IE.
		WO 2006 W:	WO 20061231 W: AE, CN, GE, KZ, MZ, SG, VN, RW: AT, IS, CF,	W0 2006123121 W: AE, AG, CN, CO, GE, GH, KZ, LC, MA, NA, SG, SK, VM, YU, RW: AT, BE, 1S, IT, CF, CG,	W: AE, AG, AL, CN, CO, CR, GE, GH, GM, KZ, LC, LK, MZ, NA, NG, SG, SK, SL, VN, YU, ZA, RW: AT, BE, BG, IS, IT, LT, CF, CG, CT,	WO 2006123121 A1 W: AE, AG, AL, AM, CN. CO, CR, CU, GE, GH, GM, HR, KZ, LC, LK, LR, MZ, NA, NG, NI, SG, SK, SL, SM, VN, YU, ZA, ZM, RW: AT, BE, BG, CH, IS, IT, LT, LU, CF, CG, CI, CM,	WO 2006123121 A1 W: AE, AG, AL, AM, AT, CN, CO, CR, CU, CZ, GE, GH, GM, HR, HU, KZ, LC, LK, LR, LS, MZ, NA, NG, NI, NO, SG, SK, SL, SM, SY, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, IS, IT, IT, IU, LV, CF, CG, CI, CM, GA,	W0 2006123121 A1 2006 W: AE, AG, AL, AM, AT, AU, CN, CO, CR, CU, CZ, DE, GE, GH, GM, HR, HU, ID, KZ, LC, LK, LR, LS, LT, MZ, NA, NG, NI, NO, NZ, SG, SK, SL, SM, SY, TJ, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, IS, IT, IT, LU, LV, MC, CF, CG, CI, CM, GA, GN,	WO 2006123121 A1 20061123 W: AE, AG, AL, AM, AT, AU, AZ, CN, CO, CR, CU, CZ, DE, OM, GE, GH, GM, HR, HU, ID, IL, KZ, LC, LK, LR, LS, LT, LU, MZ, NA, NG, NI, NO, NZ, OM, SG, SK, SL, SM, SY, TJ, TM, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, IS, IT, LT, LU, LV, MC, NL, CF, CG, CI, CM, GA, GN, GO,	WO 2006123121 A1 20061123 W: AE, AG, AL, AM, AT, AU, AZ, BA, CN, CO, CR, CU, CZ, DZ, DK, DM, GE, GH, GM, HR, HU, ID, IL, IN, KZ, LC, LK, LR, LS, LT, LU, LV, MZ, NA, NG, NI, NO, NZ, OM, PG, SG, SK, SL, SM, SY, TJ, TM, TN, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, IS, IT, LT, LU, LV, MC, NL, PL, CF, CG, CI, CM, GA, GN, GQ, GW,	WO 2006123121 A1 20061123 WO 2 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, GE, GH, GM, HR, HU, ID, IL, IN, IN, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MZ, NA, NG, NI, NO, NZ, OM, PC, LY, SG, SK, SL, SM, SY, TJ, TM, TN, TR, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, IS, IT, LT, LU, LV, MC, NL, PL, PT, CF, CG, CI, CM, GA, GN, GQ, GW, ML,	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, IS, IT, LT, LU, LV, PT, RO, CF, CG, CI, CM, GA, GQ, GW, ML, MR,	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, NZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, IS, IT, LT, LU, LV, MC, MC, PM, PL, PT, RO, SE, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,	WO 2006123121 A1 20061123 WO 2006-GB1779 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, GE, GH, GM, RR, HU, ID, IL, IN, IS, JP, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RC, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, CF, CG, CI, CM, GA, GN, GG, GW, ML, MR, NE, SN	WO 2006123121 A1 20061123 WO 2006-GB1779 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, CF, CG, CI, CM, GA, GN, GG, GM, ML, MR, NE, SN, TD,	WO 2006123121 A1 20061123 WO 2006-GB1779 2: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MA, M2, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, PG, RU, SC, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG,	WO 2006123121 A1 20061123 WO 2006-GB1779 20060 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MM, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,

GM, KE, LS, MW, MA, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
GB 2429707 A 20070307 GB 2006-18717 20060515
PRIORITY APPLN. INFO.: GB 2005-10204

WO 2006-GB1779 W - 20060515

OTHER SOURCE(S):

MARPAT 145:505473

ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) (drug candidate; prepn. of hydroxamic acids as histone deacetylase inhibitors for use against proliferative diseases including cancers) 914937-63-6 CAPLUS 5-Pyrimidinecarboxamide, 2-[6-[(3,3-diphenylpropyllamino]-3-azabicyclo[3.1.0]hex-3-yl]-N-hydroxy-(9CI) (CA INDEX NAME)

$$\mathsf{Ph}_2\mathsf{CH}-\mathsf{CH}_2-\mathsf{CH}_2-\mathsf{NH}- \overbrace{\qquad \qquad \\ \mathsf{N} \\ \downarrow \\ \mathsf{N} \\ \downarrow \\ \mathsf{C}-\mathsf{NH}-\mathsf{OH}$$

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Hydroxamic acids (shown as I; variables defined below; e.g. N-hydroxy-2-[6-[([2-naphthyl)sulfonyl]amino]-3-azabicyclo[3.1.0]hex-3-yl]pyrimidine-5-carboxamide hydrochloride (free base shown as II)) and salts, N-oxides, hydrates and solvates thereof are histone deacetylase inhibitors and are useful in the treatment of cell proliferative ases, including cancers. For I: Q, V and W = N or C; B is a divalent radical = azetidin-1,3-diyl (N on left), 3-azabicyclo[3.1.0]hexane-3,6-diyl (N on either side), hexahydropyrrolo[3,4-c]pyrrole-2,5-diyl and 3,9-diazaspiro[5.3]jundecane-3,9-diyl; A is an (un)substituted mono-, bior tri-cyclic carbocyclic or heterocyclic ring system; and -[Linkerl]-

-[Linker2]-= a bond, or a divalent linker radical; addn1. details are given in the claims. Although the methods of preparation are not

prepns. and/or characterization data for .apprx.80 examples of I are included. For example, II was prepared in 6 steps (82, not given, 85,

87 and 75 % yields, resp.) starting with condensation of tert-Bu
6-amino-3-azabicyclo[3.1.0]hexane-3-carboxylate (preparation given) with
2-naphthalenesulfonyl chloride to give tert-Bu 6-[[(2naphthyl)sulfonyl]amino]-3-azabicyclo[3.1.0]hexane-3-carboxylate, which
was deprotected and alkylated by Et 2-(methylsulfonyl)pyrimidine-5carboxylate (preparation given) to give Et
2-[6-[[(2-naphthyl)sulfonyl]amino]-3azabicyclo[3.1.0]hex-3-yl]pyrimidine-5-carboxylate, which was saponified
and

condensed with O-(1-isobutoxyethyl)hydroxylamine to give N-(1-isobutoxyethoxy)-2-[6-[[(naphthalen-2-yl)sulfonyl]amino]-3-azabicyclo(3.1.0]hex-3-yl]pyrimidine-5-carboxamide, which was cleaved by HCl to give the final product. Semiquant IC50 values for inhibition of histone deacetylase and U937, HUT and HeLa human cell lines are tabulated for .apprx.80 examples of 1. 914937-63-6P, N-Hydroxy-2-[6-(3,3-diphenylpropylamino)-3-azabicyclo[3.1.0]hex-3-yl]pyrimidine-5-carboxamide RL: PAC (Pharmacological activity): SPN (Synthetic preparation); THU (Therapeutic use): BIOL (Biological study); PREP (Preparation); USES (Uses)

WO:	A1 20061109				1	WO 2	20060501										
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH
		CN,	co,	CR,	Cυ,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD
		GE,	GH,	GM,	HR,	ΗU,	ID,	IL,	IN,	ıs,	JP,	KE,	KG,	KM,	KN,	KP,	KR
		ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	LY,	MA,	MD,	MG,	MK,	MN,	MW,	MX
		MZ,	ΝA,	NG,	NI,	NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE
		SG,	sĸ,	SL,	SM,	SY,	ŦJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC
		VN,	Yυ,	ZA,	ZM,	ZW											
	RW:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE
,		IS,	IT,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	BJ
		CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG,	BW,	GH
		GM,	ΚE,	LS,	MW,	ΜZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY
		KG,	ΚZ,	MD,	RU,	TJ,	TM										
PRIORITY	APP	LN	INFO	.:						IN 2	005-	DE18	10		A 2	0050	503

IN 2006-DE1681

OTHER SOURCE(S):

MARPAT 145:471412

AB The present invention generally relates to the present invention generally relates to the same as 1; variables defined below; e.g. N-(3-benzyl-3-azabicyclo(3.1.0)hex-6-yl)-2-hydroxy-2-phenyl-2-(2-thienyl)acetamide (1)) as muscarinic receptor antagonists, which are useful, among other uses, for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors. The invention also relates to the process for the preparation of disclosed compds.,

A 20060328

ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) pharmaceutical compns. contg. the disclosed compds., and the methods for treating diseases mediated through muscarinic receptors. For I: R1 is H or alkyl; R2 is straight or branched alkyl alkenyl, alkynyl, aryl, cycloalkyl, cycloalkylalkyl or heteroaryl (un)substituted with ≥1 alkyl, hydroxy or halogen. R3 is aryl or heteroaryl (un)substituted with ≥1 alkyl, hydroxy or halogen. R3 is aryl or heteroaryl (un)substituted with ≥1 alkyl, hydroxy or halogen; W = -(CH2)i; O = -(CH2)j; X is O or -N(R5)-; R4 is H, straight or branched alkyl, straight or branched alkenyl, aralkyl or heteroarylalkyl wherein the said aralkyl or heteroarylalkyl is further substituted with alkyl, -NH2 or alkoxycarbonylamino; R5 is H or alkyl; Rw is H or Me; and n, i, j = 0-2. Results of redioligand binding assays for M2 and M3 muscarinic receptors are reported for many examples of I. Methods of prepn. are claimed and prepns. and/or characterization data for .apprx.120 examples of I are included. For example, I was prepd. from hydroxy(phenyl) (thien-2-yl)acetic acid and 3-benzyl-3-azabicyclo[3].0)hexa-6-amine in DMF using hydroxybenzotriazole, N-methylmorpholine and I-ethyl-3-(3-dimethylaminopropyl)carbodimide.

913981-26-7P, N-(3-Benzyl-3-azabicyclo[3].1.0)hexa-6-yl)-2-hydroxy-2-phenyl-2-(2-thienyl)acetamide 913981-28-9P, N-(3-Benzyl-3-azabicyclo[3].1.0)hex-6-yl)-2-(4-finuorophenyl)-2-hydroxy-2-phenylacetamide 913981-37-0P, N-(3-Benzyl-3-azabicyclo[3].1.0)hex-6-yl)-2-(4-finuorophenyl)-2-hydroxy-2-phenylacetamide 913981-45-0P, N-(3-Benzyl-3-azabicyclo[3].1.0)hex-6-yl)-2-methoxy-2, 2-diphenylacetamide 913981-45-0P, N-(3-Benzyl-3-azabicyclo[3].1.0)hex-6-yl)-2-methoxy-2, 2-diphenylacetamide 913981-87-0P, N-(3-Benzyl-3-azabicyclo[3].1.0)hex-6-yl)-2-methoxy-2, 2-diphenylacetamide R1. PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (Clay candidate; preparation of 3,6-disubstituted sicyclo[3].1.0]hex

(Uses)
(drug candidate: preparation of 3,6-disubstituted
azabicyclo[3.1.0]hexane
derivs. as muscarinic receptor antagonists for use against

derivs. as muscarinic receptor antagonists for use against respiratory, urinary and gastrointestinal diseases) RN 913981-26-7 CAPLUS CN 2-Thiopheneacetamide, α -hydroxy- α -phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

913981-28-9 CAPLUS 3-Thiopher---31-361-26-3 CAFBO3 3-Thiopheneacetamide, α -hydroxy- α -phenyl-N-[3-(phenylmethyl)-3-azabicyclo(3.1.0)hex-6-yl]- (9CI) (CA INDEX NAME)

ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

913981-87-0 CAPLUS
Benzeneacetamide, N-3-azabicyclo[3.1.0]hex-6-yl- α -methoxy- α -phenyl- (9C1) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 10 CITED REFERENCES AVAILABLE FOR

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

$$\begin{array}{c|c} S & \begin{array}{c|c} HO & O \\ \hline & II \\ C-C-NH \end{array} \end{array} \qquad \begin{array}{c} CH_2-Ph \\ \end{array}$$

913981-36-9 CAPLUS Benzeneacetamide, 4-fluoro-α-hydroxy-α-phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

913981-37-0 CAPLUS
Benzeneacetamide, a-hydroxy-4-methyl-a-phenyl-N-(3-(phenylmethyl)-3-azabicyclo(3.1.0)hex-6-yl]- (9CI) (CA INDEX NAME)

913981-43-8 CAPLUS Benzeneacetamide, α -methoxy- α -phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

913981-45-0 CAPLUS Benzeneacetamide, N-ethyl- α -hydroxy- α -phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA İNDEX NAME)

US COPYRIGHT 2007 ACS on STN
2006-1104018 CAPLUS
146:338692
3,6-Disubstituted argaicyclo[3.1.0]hexane derivatives
as muscarinic receptor argagonists, their preparation
and use in therapy
Mehta, Anita; Dutt, Silamkot, Viswanatham Arun;
Miriyala, Bruhaspathy; Arora, Sudershan Kumar;
Srinivasulu, Boju; Mukherjee, lireshwar; Gupta, Jang
Bahadur L7 ANSWER 3 OF 8 CAPLUS ACCESSION NUMBER: 300 DOCUMENT NUMBER: 14 TITLE: 3, INVENTOR (S) Srinivasulu, Boju: Mukherjee, Bahadur Ranbaxy Laboratories Ltd., Ind Indian, 63pp. CODEN: INXXAP PARAME English PATENT ASSIGNEE(S) SOURCE: DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. DATE APPLICATION NO. KIND DATE IN 193551 PRIORITY APPLN. INFO.: 20040724 IN 2001-DE1230 IN 2001-DE1230 A1 20011207

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

The invention relates to azabicyclohexanes of general formula I, which

muscarinic receptor antagonists. In compds. I, Ar is (un) substituted

aryl or (un) substituted heteroaryl, containing 1 or 2 heteroatoms

or (un)substituted intertwarys, sometains, or carbamoyl: R2 is selected from O, S, and N; R1 is H, OH, halo, CH2OH, NH2, alkoxy, or carbamoyl: R2 is selected from C3-7 cycloalkyl, C3-7 cycloalkenyl, (un)substituted aryl, and (un)substituted heteroaryl, containing 1 or 2 heteroatoms selected from O, S, and N; W is a bond or CH2; X is a bond,

S, or N; Y is CH(R5)C(O) or (CH2)q, where R5 is H or Me and q is 0-4; R3 is H, lower alkyl, or CO2CMe3; Z is a bond, CH2, or CH2CH2; and R4 is (un) substituted saturated or unsatd. C1-15 aliphatic hydrocarbon group; dips including

pharmaceutically acceptable salts thereof. The invention also relates to the preparation of I, pharmaceutical compns. containing compds. of the invention

ntion, as well as to the use of the compns. for the treatment of respiratory, urol., and digestive diseases mediated through muscarinic receptors. Amidation of (R)-2-cyclopentyl-2-hydroxy-2-phenylacetic acid (reference

preparation is given) with azabicycle II (reference for preparation is given) gave 11 gave carboxamide III, which underwent debenzylating hydrogenation and N-alkylation with 5-bromo-2-methyl-2-pentene to give azabicyclohexane IV. The compds. of the invention are selective muscarinic antagonists, e.g., compound IV expressed 45-fold selectivity for binding to M3 receptors

12.4 nM) over M2 receptors (Ki = 564 nM) and expressed KB value of 7.95

IT

ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) in a functional assay.
712355-52-7P 712355-53-8P 712355-54-9P
712355-50-0P 712355-56-1P 712355-57-2P
712355-58-3P 712355-68-5P 712355-69-6P
712355-72-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Uses) (drug candidate; preparation of azabicyclo[3.1.0]hexane derivs. as muscarinic receptor antagonists) 712355-52-7 CAPLUS Benzeneacetamide, α -hydroxy- α -phenyl-N-[(1 α ,5 α ,6 α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

712355-53-8 CAPLUS Benzeneacetamide, 4-fluoro- α -(4-fluorophenyl)- α -hydroxy-N-[(1 α , 5 α , 6 α)-3-(phenylmethyl)-3-azabicyclo{3.1.0}hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

712355-54-9 CAPLUS Benzeneacetamide, α -phenyl-N-{{1 α ,5 α ,6 α }-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl}- α -(2-propenyloxy)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

712355-58-3 CAPLUS Benzeneacetam.de, α -phenyl-N-[{ 1α , 5α , 6α }-3-(phenylmethyl)-3-azabi-cyclo[3.1.0]hex-6-yl]- α -(2-propynyloxy)- (9CI) (CA INDEX NAVE) .

Relative stereochemistry

712355-68-5 CAPLUS
Benzeneacetic acid, α-phenyl-α-propoxy-, 2-oxo-2[{1(1,5,6)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6yl]amino]ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

$$\begin{array}{c|c} & & & \\ & & & \\$$

712355-69-6 CAPLUS Benzeneacetic acid, α -phenyl- α -(2-propenyloxy)-, 2- α - α -2-[(1 α , α , α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

712355-55-0 CAPLUS Benzeneacetamide, 4-fluoro- α -{4-fluorophenyl}-N-[(1 α , 5α , 6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- α -(2-propenyloxy)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

712355-56-1 CAPLUS Benzeneacetamide, α -phenyl-N-[{l α ,5 α ,6 α }-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- α -propoxy- (9CI) (CA INDEX NAME)

Relative stereochemistry.

712355-57-2 CAPLUS Benzeneacetamide, 4-fluoro- α -{4-fluorophenyl}-N-[(1 α ,5 α ,6 α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- α -propoxy- (SCI) (CA INDEX NAME)

Relative stereochemistry.

ANSWER 3' OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

712355-72-1 CAPLUS Benzeneacetic acid, 4-fluoro- α -(4-fluorophenyl)- α -hydroxy-, 2-oxo-2-[(1[a, 5a, 6a]-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino|ethyl ester (9CI) (CA INDEX NAME)

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2006:295302 CAPLUS DOCUMENT NUMBER: 144-350723 144-550725 Preparation of phenyl-substituted amine diols and related compounds as muscarinic receptor antagonists for treating diseases such as those of the respiratory, urinary and gastrointestinal systems Salman, Mohammad: Sarma, Pakala Kumara Savithru; Dharmarajan, Sankaranarayanan; Chug, Anita; Gupta, Suman INVENTOR(S): Suman Ranbaxy Laboratories Limited, Independent of the PCT Int. Appl., 82 pp. CODEN: PIXXD2 Patent English PATENT ASSIGNEE(S) DOCUMENT TYPE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE OTHER SOURCE(S):

CASREACT 144:350723; MARPAT 144:350723

AB This present invention generally relates to muscarinic receptor antagonists (Phc(X) (OH)C(:G)CH2N(R1)(R2) (I) or Phc(X) (OH)C(G)CH2N(R1)(R2)

(II): variables defined below; e.g.
1-cyclopentyl-3-([1,4]diazepan-1-y1)-1hydroxy-1-phenylpropan-2-one), which are useful, among other uses, for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors. The invention also relates to the process for the preparation of disclosed pharmaceutical compns. containing the disclosed compds., and the methods treating diseases mediated through muscarinic receptors. For I and II: X

ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

881206-00-4 CAPLUS 1,2-Propanediol, 1,1-diphenyl-3-[[$(1\alpha,5\alpha,6\alpha)$ -3- (phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]-, (2S)- (9CI) (CA INDEX

Absolute stereochemistry.

$$\begin{array}{c|c} OH & H \\ \hline \\ H \\ \hline \\ Ph & Ph \\ \hline \\ H \\ \end{array}$$

ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) = alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, or heterocyclylalkyl, rl = H, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy, aryloxy, -(CH2)0-2-heterocyclylalkyl, or -(CH2)0-2-heterocyclylalkyl, cycloalkyl,
a (un)satd. monocyclic or bicyclic ring system contg. 0-4 heteroatoms (O, N or S) wherein the ring can be (un)substituted with ≥ 1 of alkyl, alkenyl, alkynyl, cycloalkyl, alkaryl, alkoxy, aryloxy, et al.; G = -OR

= H or unsubstituted lower (C1-C6) alkyl], -NOR, -NHYR' (R' is H, alkyl

aryl and Y is -C(O), -SO or -SO2), or O (provided that R1 and R2 together does not form a pyrrolidine, 4-hydroxypiperidine, 4-pyrrolidinylpiperidine, piperazine or azabicyclo[3.1.0]hexane ring). Methods of prepn. are claimed and prepns. and/or characterization data

Methods of prepn. are claimed and prepns. and/or characterization data

.apprx.80 examples of I are included. For example, 1-cyclopentyl-1hydroxy-1-phenyl-3-(piperidin-1-yl)propan-2-one was prepd. (36 %) from
piperidine, Et3N and 3-bromo-1-cyclopentyl-1-hydroxy-1-phenyl-2-propanone
(prepn. described) in CH2Cl2. Ki values for I tested in a radioligand
binding assay range from .apprx.10 µM for M3 receptors,
and from .apprx.0.5 nM to .apprx.10 µM for M3 receptors. Selectivity
for bladder pressure inhibition vs. salivation was detd. for compd. 3
examples of I and was .apprx.2, similar to that detd. for tolterodine.
881098-67-5p, 3-(13-Azabicyclo[3.1.0]hex-6-yllamino]-1,1diphenylpropane-1,2-diol 881098-77-7P 881206-00-4P
RL: PAC (Pharmacological activity); SPN (synthetic preparation); USES
(Uses)

(drug candidate; preparation of Ph-substituted amine diols and related
compds. as muscarinic receptor antagonists for treating diseases such
as those of respiratory, urinary and gastrointestinal systems)
881098-675 CAPLUS
1,2-Propanediol, 3-(3-azabicyclo[3.1.0]hex-6-ylamino)-1,1-diphenyl- (9CI)
(CA INDEX NAME)

881098-77-7 CAPLUS 1,2-Fropanediol, 1,1-diphenyl-3-[{(la,5a,6a)-3-(phenylmethyl)-3-azabicyclo(3.1.0)hex-6-yl]amino}-, (2R)- (9CI) (CA

Absolute stereochemistry.

PRIORITY APPLN. INFO.: OTHER SOURCE(S):

L7 ANSWER 5 OF 8 ACCESSION NUMBER: DOCUMENT NUMBER: TITLE: S COPYRIGHT 2007 ACS on STN 2004:872781 CAPLUS 141:350045 141:350045
Preparation of substituted azabicyclo hexanderivatives as muscarinic receptor antagonis Mehta, Anita; Miriyala, Bruhapathy; Arora, Kumar; Gupta, Jang Bahadur Ranbaxy Laboratories Limited, India PCT Int. Appl., 36 pp. CODEN: PIXXD2
Patent INVENTOR (S): PATENT ASSIGNEE (S SOURCE: Instau DOCUMENT TYPE: glish FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO.

MARPAT 141:350045

10/552456

L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Title compds. I {Ar = (hetero)aryl, etc.; R1 = H, alk(en/yn)yl, etc.; R2

H, alkyl; A = $\{CH2\}$ 0-4, CO; W = $\{CH2\}$ 1-4; X = O, S, amino; Y = alkyl;

= H, alkyl, cycloalkyl, etc.] are prepared For instance, II is prepared

(3-benzyl-3-azabicyclo(3.1.0)hexan-6-yl)amine, 2-chloroacetyl chloride

(2-methoxy-5-methylphenyl)-3-phenylpropanoic acid. II exhibited pKi < 6 for both the muscarinic M2 and M3 receptors. I are useful for the treatment of respiratory, urinary and gastrointestinal disorders. 777068-38-9P 777068-40-3P 777068-58-3P 777068-64-1P RE: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); PHU (Therapeutic use); BIOI (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of substituted azabicyclo hexane derivs. as muscarinic acid.

nd
M3 receptor antagonists)
777068-38-9 CAPLUS
Benzenepropanoic acid, 2-methoxy-5-methyl-β-phenyl-,
2-oxo-2-[((lα, 5α, 6α)-3-(phenylmethyl)-3azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN ' (Continued)

777068-42-5P 777068-44-7P 777068-50-5P 777068-52-7P 777068-52-7P 777068-57-2P 777068-53-3P 777068-67-4P RL: PAC [Pharmacological activity]; SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

es; (preparation of substituted azabicyclo hexane derivs. as muscarinic

na receptor antagonists)
777068-42-5 CAPLUS
Benzenepropanamide, N-(1α,5α,6α)-3-azabicyclo[3.1.0]hex-6-yl-2-hydroxy-5-methyl-β-phenyl- (9CI) (CA INDEX NAME)

· Relative stereochemistry.

777068-44-7 CAPLUS Benzenepropanamide, N- $\{1\alpha,5\alpha,6\alpha\}$ -3-azabicyclo[3.1.0]hex-6-yl-2-methoxy-5-methyl- β -phenyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.

777068-50-5 CAPLUS
Benzenepropanoic acid, 2-methoxy-5-methyl-β-phenyl-,
2-(1(a, δa, δa)-3-azabicyclo{3.1.0}hex-6-ylamino}-2oxoethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

777068-40-3 CAPLUS

///vocatura definition acid, 5-methyl-\(\beta\)-phenyl-2-(phenylmethoxy)-, 2-oxo-2-[([da,\daggeda]-3-(phenylmethyl)-3-azabicyclo[3].10]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

777068-58-3 CAPLUS Benzenepropanamide, 2-hydroxy-5-methyl- β -phenyl-N-[(10,5x,6x)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

777068-64-1 CAPLUS

Renzenepropanamide, 2-methoxy-5-methyl-β-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L7 - ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

777068-52-7 CAPLUS
Benzenepropanoic acid, 2-hydroxy-5-methyl-β-phenyl-,
2-([1α, δα, δα]-3-azabicyclo[3.1.0]hex-6-ylamino]-2oxoethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

777068-55-0 CAPLUS Benzenepropanamide, 2-hydroxy-5-methyl-N-[2-oxo-2-[(1 α , δ _n-3-[phenylmethyl]-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl]- β -phenyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.

777068-57-2 CAPLUS Benzenepropanaide, 2-methoxy-5-methyl-N-[2-oxo-2-[[(1 α , δ c₃)-3-(phenylmethyl)-3-azabicyclo(3.1.0)hex-6-ylamino]ethyl)- β -phenyl- (9CI) (CA INDEX NAME)

Relativé stereochemistry.

ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CAPLUS ///oce-ce-3 carusa 3-Azabicyclo[3.1.0]hexan-6-amine, N-[3-(2-methoxy-5-methylphenyl)-3-phenylpropyl]-3-(phenylmethyl)-, (1α,5α,6α)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

777068-67-4 CAPLUS Phenol, 4-methyl-2-[1-phenyl-3-[[$\{1\alpha,5\alpha,6\alpha\}$ -3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]propyl]- (9CI) (CA

Relative stereochemistry.

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
NHR8CO; R8 = (CH2)r; r = 0-4; Q = (CH2)n; n = 0, 1; R6, R7 = H, Me, CO2H,
CONN2, NH2, CH2NH2; R4 = H, (substituted) (unsatd.) hydrocarbyl], were
prepd. Thus, N-{(Ia, 5a, 6a)-3-azabicyclo[3.1.0]hexan-6yl] 3,3,3-triphenylpropionamide, 4-methyl-3-pentenyl bromide, K2CO3, and
KI were stirred in DMF at 60-70° for 3 h and at room temp.
overnight to give N-[(Ia, 5a, 6a)-3-(4-methyl-3pentenyl)azabicyclo[3.1.0]hexan-6-yl] 3,3,3-triphenylpropionamide. I
bound to M2 and M3 receptors with pKi c6.
741676-03-9P 741676-04-0P 741676-05-1P
741676-02-P 741676-09-5P 741676-01-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(Claimed compound; preparation of azabicyclohexanes as muscarinic

antagonists)
741676-03-9 CAPLUS
Benzenepropanamide, β,β-diphenyl-N-[(1α,5α,6α)3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

741676-04-0 CAPLUS Benzenepropanamide, N-[(1α , 5α , 6α)-3-[4-methyl-3-pentenyl)-3-arabicyclo[3.1.0]hex-6-yl]- β , β -diphenyl- (9CI) (CA INDEX NAME)

741676-05-1 CAPLUS Benzenepropanamide, N-[$\{1\alpha,5\alpha,6\alpha\}$ -3-[2- $\{1,3\text{-benzodioxol-5-yl}\}$ ethyl $\}$ -3-azabicyclo $\{3.1.0\}$ hex-6-yl $\}$ - β,β -diphenyl- $\{9CI\}$ (CA INDEX NAME)

Relative stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2004:675748 CAPLUS DOCUMENT NUMBER: 741:207060 Preparation Preparation of azabicyclo[3.1.0]he anes as muscarinic Preparation of azabicyclo(3.1.0]hekanes as muscarin receptor antagonists Mehta, Anita; Miriyala, Bruhaspathy; Kumar, Naresh; Gupta, Jang Bahadur Ranbaxy Laboratories Limited India PCT Int. Appl., 37 pp. CODEN: PIXXD2 INVENTOR(S): PATENT ASSIGNEE(S): DOCUMENT TYPE: LANGUAGE: Patent FAMILY ACC. NUM. COUNT:

PATENT NO. KIND DATE APPLICATION NO. ATE APPLICATION NO. DATE

A1 20040819 WO 2003-18416 20030207
AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, LD, IL, IM, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LK, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO. NZ, OM, PH, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UZ, VC, VN, YU, ZA, ZM, ZW
, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, CT, CM, GA, GN, GG, GW, ML, MR, NE, SN, TD, TG
A1 20040830 AU 2003-205964 20030207
A1 20051116 EP 2003-702847
DE, DK, ES, FR, GB, GR, IT, LI, LU, NM, SE, MC, PT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EF, HU, SK
A1 20070111 (US 2006-544520 A 20030207 WO 2004069835

W: AE, AG, AL,
CO, CR, CU,
GM, HR, HU,
LS, LT, LU,
FL, PT, RO,
UA, UG, US,
RW: GH, GH, KE,
KG, KZ, MD,
FI, FR, GB,
BJ, CF, CG,
AU 2003205964
EP 1594871
R: AT, BE, CH,
IUS 2007010568
PRIORITY APPLM: INFO:: WO 2004069835

OTHER SOURCE(S):

PATENT INFORMATION:

MARPAT 111:207060 CASREACT 141:207060;

10)544520 17 Uain ArR1R2CWCOXYZNHQ

Title compds. [I; Ar = (substituted) aryl, heteroaryl; R1 = H, OH, HOCH2, aryl, alkylaryl, amino, alkoxy, carbamoyl, halo; R2 = alkyl, cycloalkyl cycloalkynl, (substituted) aryl, heteroaryl; W = (CH2)p; p = 0, 1; X = 0.00 aryl; M
S, NR, null; Y = null, CHR5CO, Me, (CH2)q; q = 0-4; R5 = H; Z = null,

ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

741676-06-2 CAPLUS Benzenepropanamide, N-[$\{1\alpha, 5\alpha, 6\alpha\}$ -3-[2-(2,3-dihydro-5-benzofuranyl)-2-oxoethyl]-3-azabicyclo[3.1.0]hex-6-yl]- β , β -diphenyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.

741676-09-5 CAPLUS Benzeneacetamide, N- $\{1\alpha,5\alpha,6\beta\}$ -3-azabicyclo[3.1.0]hex-6-yl-4-fluoro- α - $\{4$ -fluorophenyl}- α -hydroxy- $\{9CI\}$ (CA INDEX NAME)

Relative stereochemistry.

741676-10-8 CAPLUS
Benzeneacetamide, N-(1α,5α,6β)-3-azabicyclo[3.1.0]hex-6-yl-4-fluoro-α-(4-fluorophenyl)-α-propoxy- (9CI) (CA INDEX NAME)

Relative stereochemistry.

ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

741676-11-9 RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of azabicyclohexanes as muscarinic receptor antagonists) 741676-11-9 CRPLUS Benzenepropanamide, N- $\{1\alpha,5\alpha,6\beta\}$ -3-azabicyclo $\{3.1.0\}$ hex-6-yl- β , β -diphenyl- $\{9CI\}$ (CA INDEX NAME)

Relative stereochemistry.

712355-53-8P 712355-57-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of azabicyclohexanes as muscarinic receptor antagonists)
712355-53-8 CAPLUS
Benzeneacetamide, 4-fluoro-\alpha-(4-fluorophenyl)-\alpha-hydroxy-N[(10,50,60]-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6yl)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

S COPYRIGHT 2007 ACS on STA 2004:648506 CAPLUS 141:190686 Preparation of 3,6-disubstituted muscarinic receptor antagonists Mehta, Anita; Silamkoti, Arundutt Gupta, Jang Bahadur Ranbaxy Laboratories Limited, Ind PCT Int. Appl., 115 pp. CODEN: PIXXD2 Patent L7 ANSWER 7 OF 8 CAP ACCESSION NUMBER: DOCUMENT NUMBER: TITLE: zabicyclohexanes as INVENTOR (S) : PATENT ASSIGNEE(S): SOURCE: DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: Patent English

	PAT	PENT I	NO.			KIND DATE							DATE					
٠	WO 2004067510				A1 20040812			,	WO 2	003-	20030128							
		W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
			co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
			GM,	HR,	ΗU,	ID,	IL,	IN,	ıs,	JP,	KE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,
			LS,	LT,	LU,	LV,	MΑ,	MD,	MG,	MK,	MN,	MW,	MX,.	MZ,	NO,	NZ,	OM,	PH,
			PL,	PΤ,	RO,	RU,	SC,	SD,	SE,	SG,	sĸ,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,
									YU,									
		RW:							SD,									
									ΑT,									
									IT,									
									GN,									
AU 2003202727					A1		2004	0823		AU 2	003-	2027:	20030128					
	EP 1590325					A1	1 20051102				EP 2	003-	7016	20030128				
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
									MK,									
	US	2006	2472	25		A1		2006	1102		US 2	005-	5435	35 .		2	0050	727
10	RIT	APP	LN.	INFO	.:						WO 2	003-	IB25	5		A 2	0030	128

OTHER SOURCE(S):

CASREACT 141:190686; MARPAT 141:190686

10/543585

$$\begin{array}{c|c}
R^2 & R^1 & 0 \\
R^2 & R^1 & 0 \\
R^3 & Q & NR^4
\end{array}$$

Title compds. [I; Ar = (substituted) aryl, heteroaryl; Rl = H, OH, HOCH2, alkyl, amino, alkoxy, cycloalkyl, carbamoyl, halo, aryl; R2 = alkyl, cycloalkyl, cycloalkenyl, (substituted) aryl, heteroaryl; W = (CH2)p; p = 0, 1; X = 0, S, NR, null; Y = CHR5CO; R5 = H, Me, (CH2)q; q = 0-4; Q = (CH2)m; m = 0-2; R3 = H, alkyl, CO2CMe3; R4 = (unsatd.) (substituted) aliphatyl], were prepared Thus, 5-bromo-4-methylpent-3-ene, $\{1\alpha, 5\alpha, 6\alpha\}$ -b-tert-butoxycarbonylamino-3-azabicyclo[3.1.0]hexane, and K2CO3 were refluxed 5 h in MeCN to give $\{1\alpha, 5\alpha, 6\alpha\}$ -N-3-(4-methyl-3-pentenyl)-6-tert-butoxycarbonylamino-3-azabicyclo[3.1.0]hexane. This was treated with lous

Searched by Jason M. Nolan, Ph.D.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

712355-57-2 CAPLUS

Residual Re

Relative stereochemistry.

ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
HCl in EtoAc at 0 to give (1a, 5a, 6a)-N-3-(4methyl-3-pentenyl)-6-amino-3-azabicyclo(3.1.0)hexane. The latter was
stirred with 2-hydroxy-2-cyclopentyl-2-(4-methoxyphenyl)acetic acid,
hydroxybenzotriazole, N-methylmorpholine, and EDC.HCl in DMF at 0°
to room temp. to give (1a, 5a, 6a)-N-[3-(4-methyl-3pentenyl)-3-azabicyclo(3.1.0)hex-6-yl]-2-hydroxy-2-cyclopentyl-2-(4methoxyphenyl)acetamide. In a contractile assay using rat bladder
DS.

ps,

1 showed pKB = 5.08-8.36 nM.

712357-03-4P 738628-84-7P

RL: PRC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(drug candidate; preparation of 3,6-disubstituted azabicyclohexanes as muscarinic receptor antagonists)
712357-03-4 CAPLUS
Benzeneacetamide, a-phenyl-N-[{1a,5a,6a}-3-(phenylmethyl)-3-azabicyclo{3.1.0}hex-6-yl]- (9CI) (CA INDEX NAME)

738628-84-7 CAPLUS Benzeneacetamide, a-hydroxy- α -phenyl-N-[(1 α ,5 α ,6 α)-3-(1-phenylethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

IT 738629-42-0
RL: RCT (Reactant): RACT (Reactant or reagent)
(preparation of 3,6-disubstituted azabicyclohexanes as muscarinic receptor
antagonists)
RN 738629-42-0 CAPLUS
CN Benzeneacetamide, N-[(1α,5α,6α)-3-azabicyclo[3,1.0]hex-6-yl]-α-hydroxy-α-phenyl- (9CI) (CA INDEX NAME)

INVENTOR (5):

PATENT ASSIGNEE (S)

FAMILY ACC. NUM. COUNT PATENT INFORMATION:

DOCUMENT TYPE:

s muscarinic

Gupta, Jang

ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PATENT NO. KIND DATE APPLICATION NO. APPLICATION NO. DATE

WO 2002-IBS202

D20021B10

RB, BB, BB, BP, BZ, CA, CH, CN, EC, EE, ES, FI, GB, GD, GE, GH, KE, KE, KE, KE, CL, LK, LR, KM, NM, MM, MZ, NG, ND, NZ, OM, PH, S, KS, SL, TJ, TM, TM, TR, TT, TZ, ZM, ZW

BG, CH, CY, CZ, DE, DK, EE, ES, INL, FT, SE, SI, SK, TR, BF, SI, ML, MR, NR, SN, TD, TG

BU 2002-788307

JF 2004-558664

WO 2002-IB5220

A 20021210

BC 20056688

WO 2002-IB5220

A 20021210

BC 20056688 AIND DATE

A1 20040624

AL, AM, AT, AU, AZ, BA,
CU, CZ, DE, DK, DM, DZ,
HU, ID, ILI, IN, IS, JP,
LU, LV, MA, MD, MG, MK,
RO, RU, SC, SD, SE, SG,
US, UZ, VC, VN, YU, ZA,
KE, LS, MM, MZ, SD, SL,
MD, RU, TJ, TM, AT, BE,
GB, GR, IE, IT, LU, MC,
CI, CM, GA, GN, GO, GW,
A1 20040630

A1 20050914

CR, DE, DK, ES, FR, GB,
LT, LV, FI, RO, MK, CY,
T 20060817

A1 20060928

CI;
A1 20060928 WO 2004052857
W: AE, AG,
CC, CR,
GM, HR,
LS, LT,
PL, PT,
UA, UG,
RW: GH, GM, KZ,
FI, FR,
AU 2002353286
EP 1572648
R: AT, BE,
IF, SI,
JP 2006518707
VS 2006217432 WO 2004052857 OTHER SOURCE(S): CASREACT 141:714 101537857 (CH2) m N - R4

Preparation of 3,6-disubstituted arabicyclo[3.1.0]hexane derivatives

Ranbaxy Laboratories Limited, India

PCT Int. Appl., 118 pp. CODEN: PIXXD2 Patent

Bahadur

English

receptor antagonists
Mehta, Anita; Silamkoti, Arundutt Visqanatham;
Miriyala, Bruhaspathy; Arora, Sudershah Kumar;
Srinivasulu, Boju; Mukherjee, Bireshwal; Gupta

AB Title compds. I (Ar = aryl, heteroaryl, etc.; Ricycloalkyl, cycloalkenyl, aryl, heteroaryl, etc.; R2 = H, OH, amino, alkoxy, alkenyloxy, alkynyloxy,

yloxy, carbamoyl, halo; W = (CH2)p; p = 0, 1; X = 0, S, amino, no atom; Y = (CHR5)qC0, R5 = H, Me; (CH2)q; q = 0-4; m = 0-2; R3 = H, alkyl, CO2Bu-t;

ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (712355-52-7 CAPLUS Benzeneacetamide, α -hydroxy- α -phenyl-N-[(1 α , 5α , 6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

712355-53-8 CAPLUS Benzeneacetam.de, 4-fluoro- α -(4-fluorophenyl)- α -hydroxy-N-(1 α , 6 α)-3-(phenylmethyl)-3-azabicyclo{3.1.0}hex-6-yl]- (9CI) (CA INDEX NAME)

Benzeneacetamide, a-phenyl-N-[(la,5a,6a)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-a-(2-propenyloxy)- (9CI) (CA INDEX NAME)

712355-55-0 CAPLUS Benzeneacetamide, 4-fluoro- α -{4-fluorophenyl}-N-[(1 α , 5 α , 6 α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]- α -(2-propenyloxy)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) R4 = H, alkyl, etc.) and their pharmaceutically acceptable salts are prepd. The compds. of this invention can function as muscarinic receptor antagonists, and can be used for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors. The invention also relates to pharmaceutical compns. contg. the compds. of the present invention and the methods for treating the diseases mediated through muscarinic receptors. 712357-04-5P RL: PAC (Pharmacological activity); SFN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 3,6-disubstituted azabicyclohexane derivs. as muscarinic

arinic receptor antagonists) 712357-04-5 CAPLUS Benzeneactamide, N-(la,5a,6a)-3-azabicyclo[3.1.0]hex-6-yl-a-phenyl- (9CI) (CA INDEX NAME)

712357-03-4P
RL: RCT (Reactant): SPN (Synthetic preparation): PREP (Preparation): RACT (Reactant or reagent)
(preparation of 3,6-disubstituted azabicyclohexane derivs. as arinic

receptor antagonists)
712357-03-4 CAPLUS
Benzeneacetamide, α-phenyl-N-[(1α,5α,6α)-3(phenylmethyl)-3-azabicyclo{3.1.0]hex-6-yl]- {9CI} (CA INDEX NAME)

Relative stereochemistry.

IT 712355-52-7P 712355-53-8P 712355-54-9P 712355-55-0P 712355-56-1P 712355-57-2P 712355-58-3P 712355-68-5P 712355-69-6P 712335-72-1P RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of 3,6-disubstituted azabicyclohexane derivs. as muscarinic receptor antagonists)

Searched by Jason M. Nolan, Ph.D.

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) Relative stereochemistry.

RN 712355-56-1 CAPLUS
CN Benzeneacetamide, α-phenyl-N-{{1α,5α,6α}-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-propoxy-(9CI) {CA INDEX NAME}

Relative stereochemistry.

RN 712355-57-2 CAPLUS
CN Benzeneacetamide, 4-fluoro-α-(4-fluorophenyl)-N{(1α, 5α, 6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6yl]-α-propoxy- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 712355-58-3 CAPLUS
CN Benzeneacetamide, α-phenyl-N-[(1α,5α,6α)-3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]-α-(2-propynyloxy)- (9CI)
(CA INDEX NAME)

Relative stereochemistry.

RN 712355-68-5 CAPLUS
CN Benzeneacetic acid, α-phenyl-α-propoxy-, 2-oxo-2- [[(α, 50, 6α)-3-qhenylmethyl)-3-azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 712355-69-6 CAPLUS
CN Benzeneacetic acid, α-phenyl-α-(2-propenyloxy)-,
2-oxo-2-[[(la,5a,6a)-3-(phenylmethyl)-3azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

$$\begin{array}{c|c} & & & \\ &$$

RN 712355-72-1 CAPLUS
CN Benzeneacetic acid, 4-fluoro-α-(4-fluorophenyl)-α-hydroxy-,
2-oxo-2-[([α,α,6α)-3-(phenylmethyl)-3azabicyclo[3.1.0]hex-6-yl]amino]ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.